REMARKS

Claims 1, 34, 37, 40, 43-47 are pending and at issue. Claims 44 and 45 have been allowed. Please consider the following remarks:

I. Rejection Under the Judicially Created Doctrine of Obviousness-Type Double Patenting

Claims 40, 43 and 47 stand rejected under the judicially created doctrine of obviousness double patenting allegedly over claims 1-6 of U.S. Patent No. 7,179,884.

While Applicants respectfully traverse the rejection, in order to expedite prosecution toward allowance, Applicants enclose herewith a terminal disclaimer, thereby rendering this rejection moot.

II. Rejections under 35 U.S.C. §102

Claims 1, 34, 37, 40, 43, 46 and 47 are rejected under 35 U.S.C. §102(e) as being allegedly anticipated by Barker et al. (U.S. Patent Number 6,369,201). Applicant respectfully traverses the rejection as it applies to the pending claims.

The Office Action alleges, in pertinent part, that the cited reference is available as prior art because the elements as recited in the present claims (e.g. amino acids 1-20, 20 to 262 or 263, 267 or 268 to 374 of SEQ ID NOs: 2, 4, 6, 8, 10. 12. 14, 16, 18 or 20) do not enjoy the priority date of U.S. Ser. No. 09/124,180, which was filed February 18, 1998 (hereinafter, the '180 application). Hence, Barker et al., filed on February 18, 1999, antedates the present application, which was filed on July 27, 2000.

Applicants submit that the claimed elements (GDF-8 sequences) are entitled to the priority date of the '180 application, i.e., July 28, 1998. The present claims recite "amino acid residues from about 1-20 of full length promyostatin (claim 1)"; "amino acid residues from about 20 to 262 or 263 of full length promyostatin (claim 34)"; "amino acid residues from about 20 to 262 of full length promyostatin (claim 37)"; "amino acid residues from about 267 or 268 to 374

or 375 of full length promyostatin (claim 40)"; "amino acid residues from about 267 to 374 of full length promyostatin (claim 43)"; "amino acid residues from about 20 to 263 of full length promyostatin (claim 46)"; and "amino acid residues from about 268 to 375 of full length promyostatin (claim 47)".

First, with regard to claims directed to "amino acid residues from about 1-20 of full length promyostatin," support can be found in the '180 application. The predicted pre-pro-GDF-8 protein is 375 amino acids in length. Figure 2 and Example 2 of the '180 application indicates that the putative dibasic processing sites in the murine GDF-8 (myostatin) are located at "KRSRR" ('180 application, page 42, lines 18-19.) Processing of the protein precursor at this site would yield a fifteen amino acid sequence for murine GDF-8, a three amino acid sequence for human GDF-8, and a nineteen amino acid sequence for rat GDF-8. Thus, the '180 application clearly describes "amino acid residues from about 1-20 of full length promyostatin."

Second, with regard to claims directed to "amino acid residues from about 20 to 262 or 263 of full length promyostatin (claim 34)," "amino acid residues from about 20 to 262 of full length promyostatin (claim 37)" and "amino acid residues from about 20 to 263 of full length promyostatin (claim 46)" support can be found in the '180 application. In particular, Figure 5a, which shows the putative proteolytic cleavage sites at amino acids 263-267 of murine GDF-8 and Figure 5b, which shows the putative proteolytic cleavage sites at amino acids 262-266 of human GDF-8. Combining this information with the putative dibasic processing sites shown in Figure 2, processing at both sites would yield a the amino acid residues as in the above claims. Thus, the '180 application clearly describes "amino acid residues from about 20 to 262 or 263 of full length promyostatin (claim 34)," "amino acid residues from about 20 to 262 of full length promyostatin (claim 37)" and "amino acid residues from about 20 to 263 of full length promyostatin."

Third, with regard to claims directed to "amino acid residues from about 267 or 268 to 374 or 375 of full length promyostatin (claim 40)" and "amino acid residues from about 267 to

374 of full length promyostatin (claim 43)"; and "amino acid residues from about 268 to 375 of full length promyostatin (claim 47)" support can be found in Figure 5a, which shows the putative proteolytic cleavage sites at amino acids 263-267 of murine GDF-8 and Figure 5b, which shows the putative proteolytic cleavage sites at amino acids 262-266 of human GDF-8. As Example 2 of the '180 application describes, cleavage at this site would "generate a mature C terminal fragment 109 amino acids in length with a predicted molecular weight of 12,400." ('180 application, page 42, lines 19-20; see also Example 3, page 44, lines 14-16.)

Furthermore, Examples 4 and 5 of the '180 application demonstrates that the amino acid fragment from about 267 or 268 to 374 or 375 of full length promyostatin was clearly contemplated in the parental '180 application. Example 4 describe production of an anti-GDF-8 serum, which was prepared by expressing "the C-terminal region of GDF-8 (amino acids 268 to 376)" in bacteria, followed by purification of the protein and injection into rabbits to produce the antiserum. ('180 application, page 45, lines 12-14.) The antiserum detected both the unprocessed (molecular weight of 52 K) and processed (molecular weight of 15K) forms of GDF-8 expressed from stably transfected Chinese hamster ovary (CHO) cells when a Western analysis was performed under reducing conditions. ('180 application, page 45, lines 16-20.) Under non-reducing conditions, the GDF-8 antiserum detected proteins of 101K and 25K, consistent with dimeric forms of unprocessed and processed GDF-8, respectively. ('180 application, page 45, lines 21-24.)

Example 5 describes the production of a bacterial fusion construct containing a "portion of murine GDF-8 cDNA spanning amino acids 268-376" which was transformed into bacterial cells, expressed and purified. ('180 application, p. 46, lines 4-13.) The bacterially expressed, purified protein spanning amino acids 268 to 376 of GDF-8 is shown in Figure 8. This purified protein was used to immunize rabbits and chickens. ('180 application, p. 46, lines 14-16.) Western analysis of GDF-8 stably transfected CHO cells using the antiserum detected both the unprocessed (molecular weight of 52 K) and processed (molecular weight of 15K) forms of GDF-8 under reducing conditions. ('180 application, p. 46, lines 14-16.) Figure 9 shows

expression of the processed fragment (amino acids 268-376) from CHO cells that were stably transfected with GDF-8. Therefore, the parental '180 application clearly contemplates the claims of the present application.

Additionally, the '180 specification reads, in pertinent part, "alignment of the amino acid sequences of human, murine, rat, and chicken GDF-8 indicate that the sequences are 100% identical in the C-terminal biologically active fragment...Given the extensive conservation of amino acid sequences between species, it would now be routine for one of skill in the art to obtain the GDF-8 nucleic acid and amino acid sequence from any species." ('180 application, page 13, lines 11-17.) The homology of GDF-8 sequences across murine, rat, human, baboon, porcine, ovine, bovine, chicken and turkey species was also addressed in the '180 application in Example 9 and Figure 15. Figure 15b shows the amino acid alignment of GDF-8 between the eight species above. As can be seen, the amino acids sequences are highly homologous. Amino acid sequences 268-376 between 97-100% identical across the species. The claimed sequences, SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14 and 16 corresponds to SEQ ID NOS: 12, 14, 19, 21, 23, 25, 27 and 29 of the '180 application. Thus, all of the claimed sequences were contemplated in the '180 application.

Furthermore, the '180 specification reads, in pertinent part, " GDF-8 polypeptide includes functional fragments of the polypeptide, as long as the activity of GDF-8 remains. Smaller peptides containing the biological activity of GDF-8 are included in the invention ('180 application, page 12, lines 8-10.) The '180 specification also reads "one can remove amino or carboxy terminal amino acids which are not required for GDF-8 biological activity." ('180 application, page 14, lines 6-7.)

Thus, based on the foregoing, the claimed elements/sequences are supported in the '180 application and such support is enjoyed by all the disclosed GDF-8 sequences. Therefore, the claimed invention enjoys the benefit of priority of the '180 application, and the effective date for the instant amended claims *is* July 28, 1998. Because Barker et al. was filed on February 18, 1999, the reference is not available as prior art.

Accordingly, withdrawal of the rejection of the claims 1, 34, 37, 40, 43, 46 and 47 under 35 U.S.C. § 102(e) is respectfully requested.

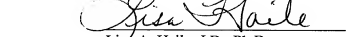
Conclusion

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this application.

The Commissioner is hereby authorized to charge the total amount of $590.00 as payment for the Terminal Disclaimer fee ($130.00) and Two-Month Extension of Time fee ($460.00), for large entity, to Deposit Account No.: 07-1896. No other fees are deemed necessary with the filing of this paper. However, the Commissioner is further authorized to charge any fees required by this submission, or credit any overpayments, to Deposit Account No. 07-1896 referencing the above-identified docket number.

Respectfully submitted,

Date: June 24, 2008



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